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Personal view

# Climate change and multiple emerging infectious diseases☆

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## Introduction

In the primordial relationship between pathogens and hosts, evolution ensures that there will always be winners and losers and, equally importantly, that such outcomes will continually change. New infectious diseases will always emerge and old threats can appear again. However, the concern is that climate change will accelerate this dynamic. Any such 'ramping up' of disease emergence offers a range of possible outcomes, from little overall impact to the occurrence of potentially catastrophic, collective disease events (del Rio Vilas et al., 2013).

Since the 1940s, the majority of emerging infectious diseases (EIDs) have originated from animal species (Cohen, 2000; Jones et al., 2008; Lloyd-Smith et al., 2009; Wood et al., 2012). Over half of the new infectious disease events from 1996 to 2009 began in Africa (Wood et al., 2012). The 'spillover' of EIDs into wider populations has been linked to host shifts and anthropomorphic driven change, ranging from globalisation, urbanisation, trade, climate and land use change to habitat fragmentation and loss of biodiversity (Lloyd-Smith et al., 2009; Cunningham et al., 2012; Morse et al., 2012; Wood et al., 2012; Woolhouse et al., 2012; Antia et al., 2013; Daszak et al., 2013).

The inter-relationship between such changes and host susceptibility and pathogen infectiousness has been the subject of much interest. For example, loss of biodiversity and the ensuing loss of host heterogeneity has been linked to disease susceptibility and transfer (Keesing et al., 2010; Meentemeyer et al., 2012). Equally, any factor that lengthens 'stochastic chains of disease transmission' allows pathogens time to adapt to their hosts, and thereby enhances disease emergence (Antia et al., 2013). Climate change is part of this rubric and, from the outset, forms the background context in which changes to occur in susceptibility and infectiousness, and, thereby, the emergence/transmission of human and animal disease.

However, the risk of multiple EIDs (MEIDs) under conditions of climate change is largely unknown. Here we describe a 'multiple disease event' as an outcome of change to the emergence/re-emergence or severity of a range of infectious diseases across both human and animal populations in any given geographical area; where the unit of interest is the collective, infectious disease burden across species. This is the aggregate of individual emerging/re-emerging diseases, including, but not limited to, those with pandemic or panzootic potential.

While studies to increase our understanding of the 'forcings' or drivers to disease states are not new, less attention has been accorded to the notion of critical environmental thresholds, as opposed to infection thresholds or related warning signals. Under conditions of climate change, such system 'features and forcings' are unlikely to act on a single disease. However, not all diseases will reach the threshold required for global spread. We know that climate change will decrease the threat of some diseases, while having little impact on others. It is possible that conditions, on balance, will support, rather than inhibit, collective disease events. As such, we are working from the hypothesis that climate change will nudge synergies and interactions between drivers, and between diseases themselves, forging a 'cascade effect' that may ultimately result in MEIDs. While a cascade builds energy and momentum over time, similarly climate change may forge conditions for MEIDs. If so, this raises a variety of questions. Firstly, can we identify, a priori, the cascade of factors that might alter the composition and/or frequency of occurrence of such collective disease events? Secondly, can we calculate the related risk? Finally, on a broader level, will such cascades provide warning signs of wider systems change?

However, explorations of such cascades are likely to place new demands on both conceptual and methodological approaches to infectious disease and climate change (Heffernan et al., 2012). The dominant concept of climate change is as a unique and discreet driver of disease amongst a range of other drivers, including economic, social and ecological factors (Chomel, 2008; Heffernan et al., 2012; Antia et al., 2013; Heffernan, 2013a,b).[1] This conceptual notion has forged a related approach, which focusses on disaggregating the explicit impact of particular drivers on specific diseases. Such an approach is less useful in identifying the

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[1] See: https://www.gov.uk/government/publications/infectious-diseases-preparing-for-the-future (accessed 1 January 2018).

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synergies between such drivers and their role in collective, as opposed to singular, disease events.

On the analytical level, our most straightforward disease models start from the incidence and prevalence of a disease and work backwards to elucidate the wide range of factors, and their inter-relationships, that influence pathogens over time and space (Polley and Thompson, 2009; Meentemeyer et al., 2012; Antia et al., 2013).

Central to modelling infectious disease is the concept of R0 or 'the basic reproduction number', where R0 is the expected number of secondary infections caused by a single infected individual within a susceptible population for the period of infection (Keeling and Rohani, 2008; Gumel and Lenhart, 2010; Antia et al., 2013). An $R0 > 1$ supports an epidemic, while $R0 < 1$ predicts that a disease will die out. In this manner, R0 is a threshold, as opposed to a scale or strength, value. For vectors and some parasites, R0 refers to '*the average number of female offspring produced throughout the lifetime of a mature female . . . which themselves achieve reproductive maturity, in the absence of density-dependent constraints*' (Gumel and Lenhart, 2010). Calculations of R0 are then linked to general habitat conditions such as the normalised difference vegetative index (NDVI), surface hydrology and temperature data, the latter via remote sensing (RS) and geographical information systems (GIS) (Mas-Coma et al., 2008). The parameters are applied to simulation models to create predictions/scenarios of a vector population and, hence, dynamics of a particular vector-borne disease under conditions of climate change. Such work has been vital to understanding the role of different drivers, particularly climate change, in disease outcomes.

Could R0 help us in predicting wider system changes? More specifically, could an aggregate R0 calculation aid in the quest for an early warning system for MEIDs (Shuman, 2010)? In relation to the systems concept of a tipping point, calculations of R0, which estimate infectiousness, may be viewed as 'bifurcation' measures, where a single disease 'tips' from one state to another. However, the calculation offers little insight into the 'tipping elements' (here the 'forcings' of the system or the inter-relationship of factors driving such change). On the face of it, R0 may be a better 'outcome' than 'predictive' measure. Recently, it has been hypothesised that $R0 < 1$ can still be important in contributing to the conditions required for the emergence of an epidemic (Antia et al., 2013). This is important given what is increasingly recognised as the non-linearity of disease processes (Reperant, 2010; Woolhouse, 2011).

Conversely, in relation to vectors, R0 may be viewed as a 'predictive' measure (which includes a range of climate variables) of the potential exposure to a vector and thereby vector-borne disease. However, estimating with accuracy the link between vector populations and host infections is often difficult (Baylis, 2013). As such, for vector-borne diseases, R0 may lack the characteristics required to be either a 'bifurcation' or 'outcome-based' measure of the disease or system. Clearly the aggregate of individual disease R0 values could offer at least an approximate indicator of the collective epidemic/panzootic potential in any given geographical area. While important, such an approach will be less useful in helping us to predict the constellation of factors important to the emergence of MEIDs in the first place.

The 'new' challenges posed by climate change require a robust and holistic approach to understanding disease dynamics (Altizer et al., 2013; McMichael, 2013). Our present understanding of the indirect effects of climate change on disease transmission and the interactive, potentially synergistic, effects with a range of other disease drivers remains a crucial gap. At least part of the problem is that including human factors in climate models remains technically challenging (Bennema et al., 2011). Thus, accurately assessing disease risks and/or mitigating factors can be difficult (Morgan and Wall, 2009). Furthermore, many of the socio-economic impacts of climate change are 'uncertain' (Stone, 2008). While scale is an issue for incorporating climate data into disease models (Bennema et al., 2011; Meentemeyer et al., 2012), it is equally problematic in attempts to model climate, disease and behavioural/management effects.

At the macro-level, the factors involved in collective disease 'spillovers' are not likely to be equal in importance, given the expected impacts of climate change on developing communities in the 'Global South' (Africa, Latin America and South-East Asia and the Middle East). Anticipated large-scale shifts in demographics, urbanisation and agricultural production (Thornton et al., 2009; Lobell et al., 2011; Muller et al., 2011) will influence the geographical location of host and pathogen populations and, ultimately, the particular collection of diseases involved.

## Climate change and disease cascades

Within the Global South, climate change is likely to have a primary impact on crop and livestock production, with secondary impacts on food and livelihood security. From these outcomes and impacts, alterations in poverty levels and human behaviour will arise, including adaptation and coping mechanisms, ultimately resulting in demographic and production shifts. In turn, these shifts will have a primary impact on host/pathogen interactions, including susceptibility and infectiousness, and, ultimately, the emergence/re-emergence and geographical spread of human and animal disease (Fig. 1).

It may be argued that climate change creates a 'cascade effect' on the factors important to the emergence/re-emergence of disease. Understanding such disease cascades requires a shift from 'outcome' to 'cascade' measures, where cascade measures are defined as incremental impacts and influences of change across the biological, social and wider environmental factors important to identifying the interplay between climate change and disease. Across the cascade, variables can be either positive or negative (and in some cases neutral) with regard to shifting host populations and production parameters (Table 1).

Such a cascade clearly meets the criteria for identifying the cumulative effect/threshold or tipping point for the collective emergence/re-emergence of infectious diseases. However, while such demographic and production shifts may indicate the likely locality of disease events, they tell us little of susceptibility or infectiousness. Rather, infectiousness and susceptibility are derived from a range of factors that may act as synergists, mitigators or amplifiers on hosts and pathogens.

## Synergists, amplifiers and mitigators

Within this context, a 'synergist' may be viewed as a combination of abiotic or biotic factors that act in tandem to change disease processes. In this manner, a synergist can be any two or more elements related to the pathogen, wider environment, climate or the host that alter the manifestation or distribution of a disease. Many synergists in the transmission of infectious disease are known; for example, warming temperatures and subsequent changes to vector physiology act as synergists in the spread of vector-borne disease. While the notion of biotic synergists on disease processes is not new, the role of abiotic synergists, such as cultural, economic or social factors amplifying disease effects or transmission processes within a context of climate change, has been less well explicated.

Conversely, an amplifier singularly enhances disease processes. Again, there are many examples of both abiotic and biotic amplifiers. The severe acute respiratory syndrome (SARS) pandemic offers a good example of the amplifying effect of global travel (Ruan et al., 2006). Alternatively, early in the H5N1 highly

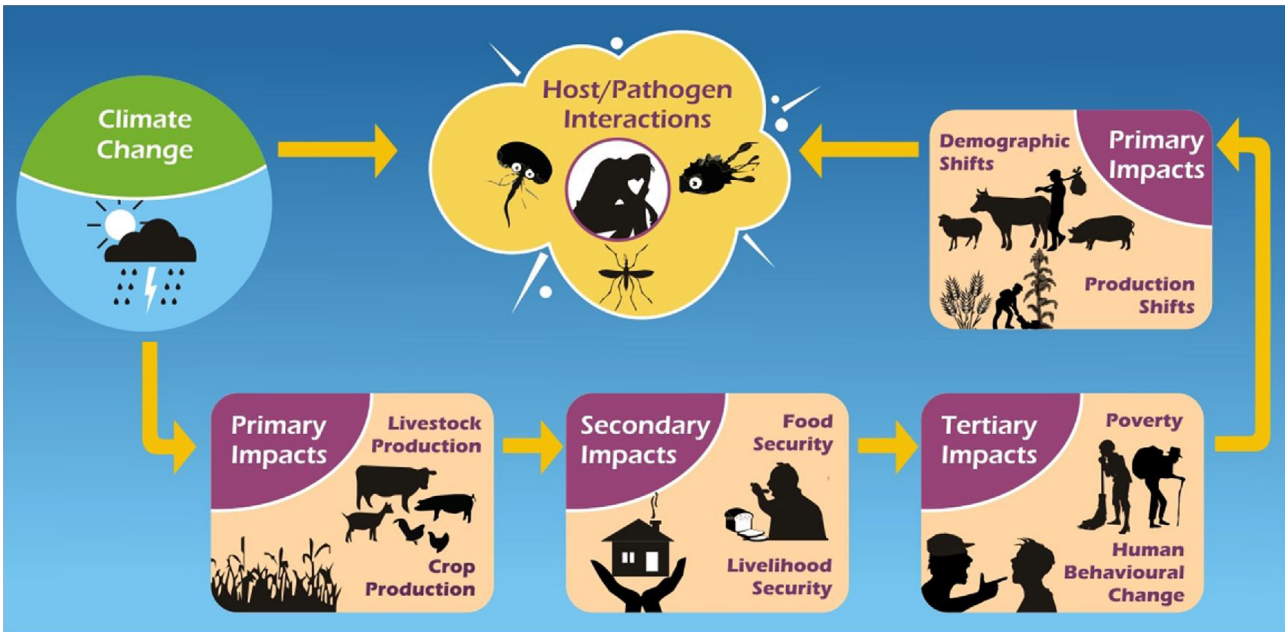


**Fig. 1.** The infectious disease climate change cascade. Climate change has a range of primary impacts on host/pathogen interactions and wider agricultural production, with secondary and tertiary impacts on livelihoods and behaviour, leading to demographic shifts, which equally have an impact on host/pathogen interactions.

**Table 1**
Variables under flux due to climate change.

| Variable | Positive | Negative |
|---|---|---|
| Crop yields | Increasing yields (site and species specific) | Decline in yields (site and species specific) |
| Livestock herds | Lower densities, low carbon livestock development, sustainable management strategies | Decline in available grazing<br>Decrease in herd size |
| Food security | Increase in livestock outputs/crop yields | Decline in livestock outputs/crop yields |
| Livelihood security | Increased livelihood opportunities due to changing environments/ geographies | Decline in on-farm income, loss of labour due to out migration. |
| Poverty | Rise in income due to positive livelihood changes | Decline in overall household income |
| Human behaviour change | Adaptation strategies, technology adoption, adoption of disease control measures | Maladaptive strategies, natural resource destruction/over-use |
| Migration | Shifts in human and animal population densities in rural areas | Shifts in rural/local population, increased urbanisation |
| Production shifts | Shifts in climate compatible production, crop and livestock species/ geographical areas | Shifts in crop and livestock species/geographical areas<br>Shifts in management strategies i.e. increased livestock density |
| Host/pathogen/vector interactions | Shifts in host/pathogen/vector species and population density, bio- diversity | Shifts in host/pathogen/vector species and population density, biodiversity |

pathogenic avian influenza (HPAI) panzootic, wild bird migration was offered as a key amplifier. Latterly, the illegal global trade in poultry was found to be a more potent factor in spread (Wei et al., 2013).

Mitigators are factors that decrease disease processes. Effective mitigators can over-ride both synergists and amplifiers; for example, smallpox was eradicated globally via the creation and delivery of an effective vaccine. Rinderpest was also eradicated largely due to the creation of a thermo-stable vaccine working in tandem with an effective delivery system (Mariner et al., 2012) While mitigators may be largely viewed as technologies, there are many abiotic and biotic forces that can also decrease disease transmission. Although warming temperatures may amplify some infectious diseases, such increases may act to mitigate others, and these factors may differ by geographical area (even for the same disease) (Lloyd-Smith et al., 2009; Woolhouse et al., 2012).

Identifying synergists and amplifiers, as opposed to mitigators, can reveal those diseases with the greatest risk of global spread and those with the greatest potential for containment. An exploration of four critical human and animal diseases from this perspective reveals the synergists, amplifiers and mitigators of infection (Table 2). On a practical level, such an approach effectively sets priorities for, and thereby limits or ring fences, the data requirements of future models. Furthermore, the focus on disease synergists, amplifiers and mitigators enables the use and re-application of a wide body of existing data.

Each of the above factors has a greater or lesser proportional impact on the disease in question. Equally importantly, all of the factors may reach a level where no further impact or gains may be derived. For example, while poverty is related to the incidence of malaria, the depth of poverty has little further proportional impact on disease levels. In relation to mitigators, such as bed nets, proportional gains in prevention are directly linked to distribution or coverage levels. Disaggregating the proportional impact of such factors on disease outcomes may ultimately enable priorities of human and animal disease to be set within a context of climate change.

## Towards a new episteme and community of practice

Within the field of global health, currently there is a consensus on the need for multi-disciplinary approaches and investigations.

**Table 2**
Examples of synergists, amplifiers and mitigators.

| Disease | Synergists | Amplifiers | Mitigators |
|---|---|---|---|
| Malaria | Climate change, increased temperature, rainfall | Poverty, lack of healthcare services, low levels of disease prevention awareness, human mobility | Bed nets, seasonal malaria chemo-prevention, use of insecticides, future application of genetically modified vaccine candidates, levels of urbanisation |
| Dengue | Climate change, increased temperature, rainfall | Passive international transport, i.e. tyre trade, lack of healthcare services, low levels of disease prevention awareness, localised human movement across social networks, migration, domestic and international travel | Insecticide use, application of larvicides, environmental clean-up, reduction of breeding sites/water containers, genetic modification of male mosquitoes (sterile males), mosquito nets, biological agents, e.g. mesocyclops |
| Rift Valley fever | Climate change, El Niño Southern Oscillation (ENSO) | Close proximity to infected livestock, increased livestock trade from endemic areas | Insecticide use, vector control strategies, high uptake of Rift Valley fever vaccine, effective early warning systems, lowering animal exposure rates during outbreaks |
| East Coast fever | Climate change, increased temperature, rainfall Changing distribution of vectors, e.g. *Rhipicephalus appendiculatus* | Low levels of vaccine adoption, low/ineffective levels of acaricide use, acaricide resistance, management changes, disruption to endemic stability, increasing tick challenge | Development of effective and easily administered vaccines, production system change/ intensification, management changes, lowering tick challenge, enhancing indigenous animal genetic resources (AnGR) |

This has forged important work on explorations of single diseases from multiple disciplines and perspectives, yielding a better understanding of drivers, pathways, causes and the targeting of responses. Climate change, as a background context, forces us to consider disease at the collective level. It is at this level that the synergies and interactions, within and between drivers to both human and animal disease, take on increasing importance.

A unifying framework upon which to build a community of practice is required to make such an approach practical. Explorations of zoonoses and diseases with an impact on public health generally fall under the rubric of 'One Health', which explores the interface between human and animal disease and the environment. Conversely, synergies in disease dynamics fall under the concept of 'syndemics', where a syndemic is defined as '*two or more afflictions, interacting synergistically, contributing to excess burden of disease in a population*' (Rock et al., 2009; Heffernan, 2013a,b). Neither concept offers us a clear direction for delineating the implicit and indirect roles of climate change in forging MEID events.

Instead, by identifying the synergists, amplifiers and mitigators to human and animal disease, we can begin to classify and set priorities for the constellation of factors important to the formation of potential 'tipping points' in Global Health status. This is fundamental in being able to prevent such critical points developing. Critical to this approach is delineating the 'cascade effect' of particular events on this collective disease potential. Thus, changing our outlook from a linear progression, where discreet drivers influence a particular disease, to a model where the interaction of particular drivers creates a 'cascade effect', will help us to identify a range of 'bifurcation points' that lead ultimately to MEIDs.

Presently, there is a large volume of existing global human and animal health data available to aid this task. The global move to make much of these data open access is underway and will greatly aid this end; examples of organisations promoting this approach include the Wellcome Trust and the World Health Organization (WHO). Furthermore, collaborative efforts to forge active data collection/sharing at the global level, such the global early warning system (GLEWS) network for health threats at the human-animal ecosystem interface, is a step in the right direction. Such collaborative networks form the basis for joint risk identification and data sharing[2] (FAO, OIE, WHO, 2013). Hence, our starting point is to utilise existing data to reconfigure our outlook on MEIDs, climate change and global health. Such an approach will also help to identify those human and animal diseases with the highest 'spillover' potential and thereby aid priority setting and resource allocation in the coming decades.

[2] See: http://www.glews.net/wp-content/uploads/2013/12/04_GLEWSConcept-20-11.pdf (accessed 1 January 2018).

## Conflict of interest statement

The author of this paper has no financial or personal relationship with other people or organisations that could inappropriately influence or bias the content of the paper.

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